

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	113	leptin same angiopoietin	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:21
L2	9	leptin same angiopoietin.cdm.	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:23
L3	65	leptin same angiopoietin and angiogenesis	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:24
L4	6	I3 and @py<"2003"	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:34
L5	41	rubinstein near menachem	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:35
L6	3	cohen near batya	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:35
L7	7	I5 and leptin	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:35
L8	0	I5 and leptin and angiopoietin	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:35
L9	7	I7	US-PGPUB; USPAT; DERWENT	OR	ON	2006/09/11 16:35

=> d his

(FILE 'HOME' ENTERED AT 16:39:01 ON 11 SEP 2006)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 16:39:24 ON 11 SEP 2006

L1           5 S LEPTIN WITH ANGIOPOIETIN  
L2           0 S LEPTIN SAME ANGIOPIETIN  
L3          4284 S ANGIOPOIETIN  
L4         36486 S LEPTIN  
L5           49 S L3 (L) L4  
L6           18 S L5 AND ANGIOGENESIS  
L7           12 DUP REM L6 (6 DUPLICATES REMOVED)  
             E RUBINSTEIN MENCHEN /AU  
L8          251 S E1  
             E COHEN BATYA /AU  
L9           38 S E3  
L10         269 S L8 OR L9  
L11          16 S L10 AND LEPTIN  
L12           4 S L11 AND ANGIOPOIETIN  
L13          3 DUP REM L12 (1 DUPLICATE REMOVED)

=>

L7 ANSWER 1 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 TI Angiogenesis soluble factors (ASF) correlate with markers of  
 fibrosis (ME) and histological lesion in chronic hepatitis C patients.  
 AU Salcedo-Mora, Xamila B.; Sanz-Cameno, Paloma; Medina, Jesus;  
 Martin-Vilchez, Samuel; Garcia-Buey, Luisa; Trapero, Maria;  
 Gomez-Dominguez, Elena; Moreno-Moteagudo, Jose Andres; Borque, Maria  
 Jesus; Rubio, Saioa; Mendoza, Jorge; Legido, Jesus; Gisbert, Javier P.;  
 Moreno-Otero, Ricardo  
 PY 2005  
 SO Gastroenterology, (APR 2005) Vol. 128, No. 4, Suppl. 2, pp. A712-A713.  
 Meeting Info.: Annual Meeting of the American-Gastroenterological-  
 Association/Digestive-Disease-Week. Chicago, IL, USA. May 14 -19, 2005.  
 Amer Gastroenterol Assoc.  
 CODEN: GASTAB. ISSN: 0016-5085.

L7 ANSWER 2 OF 12 MEDLINE on STN DUPLICATE 1  
 TI Adipose tissue angiogenesis.  
 AU Hausman G J; Richardson R L  
 PY 2004  
 SO Journal of animal science, (2004 Mar) Vol. 82, No. 3, pp. 925-34. Ref: 61  
 Journal code: 8003002. ISSN: 0021-8812.

L7 ANSWER 3 OF 12 MEDLINE on STN DUPLICATE 2  
 TI Differential expression of angioregulatory factors in normal and  
 CNV-derived human retinal pigment epithelium.  
 AU Martin Gottfried; Schlunck Gunther; Hansen Lutz L; Agostini Hansjurgen T  
 PY 2004  
 SO Graefe's archive for clinical and experimental ophthalmology = Albrecht  
 von Graefes Archiv fur klinische und experimentelle Ophthalmologie, (2004  
 Apr) Vol. 242, No. 4, pp. 321-6. Electronic Publication: 2004-01-14.  
 Journal code: 8205248. ISSN: 0721-832X.

L7 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN  
 TI Progress in mechanism of corneal neovascularization  
 AU Liao, Qiong  
 PY 2004  
 SO Yanke Yanjiu (2004), 22(2), 213-215  
 CODEN: YAYAFH; ISSN: 1003-0808

L7 ANSWER 5 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 TI Regulation of wound healing by growth factors and cytokines.  
 AU Werner, Sabine [Reprint Author]; Grose, Richard  
 PY 2003  
 SO Physiological Reviews, (July 2003) Vol. 83, No. 3, pp. 835-870. print.  
 ISSN: 0031-9333 (ISSN print).

L7 ANSWER 6 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 TI Leptin receptors on human hepatic stellate cells mediate the expression of  
 pro-inflammatory and pro-angiogenic cytokines.  
 AU Aleffi, Sara [Reprint Author]; Petrai, Ilaria [Reprint Author]; Caligiuri,  
 Alessandra [Reprint Author]; Laffi, Giacomo [Reprint Author]; Pinzani,  
 Massimo [Reprint Author]; Gentilini, Paolo [Reprint Author]; Marra, Fabio  
 [Reprint Author]  
 PY 2003  
 SO Hepatology, (October 2003) Vol. 38, No. 4 Suppl. 1, pp. 776A. print.  
 Meeting Info.: 54th Annual Meeting of the American Association for the  
 Study of Liver Diseases. Boston, MA, USA. October 24-28, 2003. American  
 Association for the Study of Liver Diseases.  
 ISSN: 0270-9139 (ISSN print).

L7 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 3  
 TI Adipose tissue growth and regression are regulated by angiopoietin-1.  
 AU Dallabrida Susan M; Zurakowski David; Shih Shu-Ching; Smith Lois E;  
 Folkman Judah; Moulton Karen S; Rupnick Maria A

PY 2003  
 SO Biochemical and biophysical research communications, (2003 Nov 21) Vol. 311, No. 3, pp. 563-71.  
 Journal code: 0372516. ISSN: 0006-291X.

L7 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN  
 TI Leptin for use in inhibition of endothelial cell proliferation optionally together with VEGF inhibitors  
 IN Rubinstein, Menachem; Cohen, Batya; Barkan, Dalit  
 PY 2001  
 2001  
 2001  
 2001  
 2005  
 2002  
 2002  
 2003  
 2003  
 2003  
 2002  
 2005

SO PCT Int. Appl., 38 pp.  
 CODEN: PIXXD2

L7 ANSWER 9 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 TI Similarities between cardiac and adipose tissue vascular remodeling.  
 AU Rupnick, Maria [Reprint author]; Dallabrida, Susan; Panigrahy, Dipak; Nunn, Michelle; Langer, Robert; Folkman, Judah  
 PY 2001  
 SO Circulation, (October 23, 2001) Vol. 104, No. 17 Supplement, pp. II.K. print.  
 Meeting Info.: Scientific Sessions 2001 of the American Heart Association. Anaheim, California, USA. November 11-14, 2001. American Heart Association.  
 CODEN: CIRCAZ. ISSN: 0009-7322.

L7 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN  
 TI New molecular mediators in tumor angiogenesis  
 AU Beecken, W.-D.; Kramer, W.; Jonas, D.  
 PY 2000  
 SO Journal of Cellular and Molecular Medicine (2000), 4(4), 262-269  
 CODEN: JCMMC9; ISSN: 1582-1838

L7 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN  
 TI Modulation of angiogenesis and wound healing using an agent that modulates leptin or leptin receptor mediated angiogenic response  
 IN Sierra-Honigmann, Rocio M.  
 PY 1999  
 1999

SO PCT Int. Appl., 89 pp.  
 CODEN: PIXXD2

L7 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
 TI Science, medicine, and the future: Therapeutic angiogenesis.  
 AU Henry, Timothy D. [Reprint author]  
 PY 1999  
 SO BMJ, (June 5, 1999) Vol. 318, No. 7197, pp. 1536-1539. print.  
 ISSN: 0959-8138.

=> d 17 5-7 kwic

L7 ANSWER 5 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

IT . . . . . integumentary system, migration; skin: integumentary system

IT Diseases  
wound: injury

IT Chemicals & Biochemicals  
HB-epidermal growth factor: expression; activins: expression;  
angiopoietins: expression; bone morphogenetic proteins:  
expression; chemokines: expression; connective tissue growth  
factor/cysteine-rich 61/nephroblastoma overexpressed family; cytokines;  
epidermal growth factor family: expression; fibroblast growth factor  
family; granulocyte-macrophage colony stimulating factor: expression;  
growth factors; insulin-like growth factors: expression;  
interleukin-10: expression; leptin: expression; nerve growth  
factor: expression; platelet-derived growth factor family;  
proinflammatory cytokines: expression; scatter factors: expression;  
transforming growth factor-beta: expression; vascular. . . .

IT Miscellaneous Descriptors  
angiogenesis; late-stage wound repair; reepithelialization;  
scarring; wound healing: regulation

RN 114949-22-3Q (activins)  
288154-25-6Q (activins)  
250740-90-0 (angiopoietins)  
83869-56-1 (granulocyte-macrophage colony stimulating factor)  
61912-98-9 (insulin-like growth factors)  
169494-85-3 (leptin)  
9061-61-4 (nerve growth factor)

L7 ANSWER 6 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AB Recent investigation has indicated a role for leptin as a  
profibrogenic agent during chronic liver damage, as shown by reduced  
collagen accumulation and TGF-beta expression in animals deficient in  
leptin or its receptors. However, the cellular targets of  
leptin's action within the liver have not been completely  
elucidated, and all available data have been obtained in rodent models.  
Aim of the present study was to investigate the expression and function of  
leptin receptors (ObR) in human cultured hepatic stellate cells  
(HSC) and to correlate receptor activation with biologic actions relevant  
for the. . . abundant in freshly-isolated HSC, indicating that  
increased expression of ObR parallels acquisition of an activated  
phenotype. Exposure of HSC to leptin (200 ng/ml) increased the  
levels of tyrosine kinase activity associated with the receptors, as  
indicated by immune complex kinase assays.. . . of approximately 125  
kDa, possibly represented by Jak2, in analogy with other cell systems. In  
agreement with this observation, in leptin-stimulated HSC, a  
marked increase in the phosphorylation of Stat3, a molecule activated by  
different kinases, including Jak2, was observed. Activation of  
leptin receptors also induced the activation of different members  
of the mitogen-activated protein kinase family, such as p38MAPK and ERK,  
and of Akt, a kinase downstream of PI3K. To establish the possible  
activation of transcription factors, nuclear extracts from leptin  
-stimulated HSC were analyzed in electrophoretic mobility assays. With  
this technique, increased binding of nuclear proteins to consensus  
oligonucleotides for NF-kappa B, Stat3, and AP-1 was observed. We next  
evaluated whether leptin induces pro-inflammatory actions in  
HSC, analyzing the expression of MCP-1, a chemokine that targets monocytes  
and lymphocytes, at the gene and protein levels. A dose-dependent  
increase in MCP-1 mRNA was evident in leptin-stimulated cells,  
together with increased accumulation of this chemokine in the culture  
supernatant. The increase in MCP-1 expression was blocked by. . .  
pharmacologic inhibitors of Jak2 or p38MAPK activation, but not by  
inhibitors of the ERK pathway. Finally, exposure of HSC to leptin  
increased the levels of mRNA encoding for VEGF and angiopoietin  
-1, which participate in the process of neo-angiogenesis. We  
conclude that human activated HSC express functional leptin

receptors, the activation of which transduces intracellular signals. ObR activation is associated with increased expression of pro-inflammatory and pro-angiogenic cytokines, indicating a complex role of leptin in the regulation of the liver wound-healing response.

IT

and lymphatics, immune system

IT

Chemicals & Biochemicals

AP-1; ERK [cb]: Akt; Jak2; MCP-1: expression; NF-kappa B; PI3K; Stat3; VEGF; angiopoietin-1; leptin receptor; p38MAPK; tyrosine kinase

L7

ANSWER 7 OF 12

MEDLINE on STN

DUPLICATE 3

AB

Adipose tissue is unique in its plasticity, capacity for vascular remodeling, and susceptibility to angiogenesis inhibitors. We hypothesize that these characteristics are enabled by maintaining relatively immature adipose vessels to facilitate vascular/tissue remodeling. We examined the vascular maturation regulators, angiopoietin-1, angiopoietin-2, and tie2 receptor, under different weight-modifying conditions. Adipocytes expressed angiopoietin-1, while adipose endothelial cells expressed angiopoietin-2 and tie2. Adipose tissue growth/regression were associated with decreased angiopoietin-1 mRNA and protein, and tie2 phosphorylation. Angiopoietin-2 and tie2 mRNA levels were stable. Angiopoietin-1 mRNA levels inversely correlated with the rates of change in body weight, independent of the direction (weight gain, loss) or etiology (TNP-470, leptin, and diet restriction) of the weight shift. Obese mice injected with ang1/pcDNA had reduced rates of weight gain and fat pad weights, regardless of the route of plasmid administration (subcutaneous, intramuscular, and intravenous). Thus, angiopoietin-1 may regulate adipose tissue growth, suggesting that vascular maturation alters tissue plasticity.

=> d 17 9-10 12 kwic

L7

ANSWER 9 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

IT

IT

Diseases

obesity: nutritional disease

Obesity (MeSH)

IT

Chemicals & Biochemicals

Bay 12-9566; TNP-470: cardiovascular-drug; adn-flk; ang-1 [angiotensin-1]: expression; ang-2 [angiotensin-2]; angiopoietin-1: vessel destabilizer; angiopoietin-2: vessel destabilizer; angiopoietin-2 mRNA [angiopoietin-2 messenger RNA]: expression; angiostatin; endostatin; leptin; tie-2

IT

Miscellaneous Descriptors

angiogenesis regulation; vascular maturity; vascular remodeling regulation; Meeting Abstract

RN

179545-77-8 (Bay 12-9566)

129298-91-5 (TNP-470)

186270-49-5 (angiopoietin-1)

194368-66-6 (angiopoietin-2)

86090-08-6 (angiostatin)

187888-07-9 (endostatin)

169494-85-3 (leptin)

L7

ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN

TI

New molecular mediators in tumor angiogenesis

AB

A review, with 67 refs. Angiogenesis is essential for tumor growth and progression. It has been demonstrated that tumor growth beyond a size 1 to 2 mm<sup>3</sup> requires the induction of new vessels. Angiogenesis is regulated by several endogenous stimulators and

inhibitors of endothelial cell migration, proliferation and tube formation. Under physiol. conditions these. . . disease in several tumor entities. Within the last years several new mediators of endothelial cell growth have been isolated e.g. angiopoietin 1, angiopoietin 2, midkine, pleiotrophin, leptin and maspin. In this review we discuss the mechanisms leading to tumor angiogenesis and describe some of the newer mediators of endothelial cell stimulation and inhibition.

ST review tumor angiogenesis angiopoietin midkine  
pleiotrophin leptin maspin  
IT Angiogenesis  
Neoplasm  
(mol. mediators in tumor angiogenesis)  
IT Midkines  
Pleiotrophins  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(mol. mediators in tumor angiogenesis)  
IT 157857-21-1, Maspin 169494-85-3, Leptin 186270-49-5, angiopoietin 1  
194368-66-6, angiopoietin 2  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(mol. mediators in tumor angiogenesis)  
L7 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN  
TI Science, medicine, and the future: Therapeutic angiogenesis.  
IT .  
disease  
Myocardial Infarction (MeSH)  
IT Diseases  
myocardial ischemia: heart disease, vascular disease  
Myocardial Ischemia (MeSH)  
IT Chemicals & Biochemicals  
angiogenic growth factors; angiopoietin; fibroblast growth  
factor; granulocyte colony stimulating factor; hepatocyte growth  
factor; insulin-like growth factor; interleukin-8; leptin;  
placental growth factor; platelet-derived growth factor; proliferin;  
thyroxine; transforming growth factor-alpha; transforming growth  
factor-beta; tumor necrosis factor-alpha; vascular endothelial growth.  
IT Methods & Equipment  
therapeutic angiogenesis: therapeutic method  
IT Miscellaneous Descriptors  
clinical trials; pathological angiogenesis  
RN 250740-90-0 (angiopoietin)  
62031-54-3 (fibroblast growth factor)  
143011-72-7 (granulocyte colony stimulating factor)  
61912-98-9 (insulin-like growth factor)  
169494-85-3 (leptin)  
92769-12-5Q (proliferin)  
152469-17-5Q (proliferin)  
51-48-9 (thyroxine)  
127464-60-2 (vascular endothelial growth factor)

=> d his

(FILE 'HOME' ENTERED AT 16:39:01 ON 11 SEP 2006)

FILE 'MEDLINE, CAPLUS, BIOSIS' ENTERED AT 16:39:24 ON 11 SEP 2006

L1 5 S LEPTIN WITH ANGIOPOIETIN  
L2 0 S LEPTIN SAME ANGIOPOIETIN  
L3 4284 S ANGIOPOIETIN

L4 36486 S LEPTIN  
 L5 49 S L3 (L) L4  
 L6 18 S L5 AND ANGIOGENESIS  
 L7 12 DUP REM L6 (6 DUPLICATES REMOVED)

=> e rubinstein menchem /au

E1 251 RUBINSTEIN MENACHEM/AU  
 E2 3 RUBINSTEIN MENACHEM/AU  
 E3 1 --> RUBINSTEIN MENACHEM/AU  
 E4 123 RUBINSTEIN MICHAEL/AU  
 E5 1 RUBINSTEIN MICHAEL A/AU  
 E6 1 RUBINSTEIN MICHAEL C/AU  
 E7 70 RUBINSTEIN MICHAEL H/AU  
 E8 15 RUBINSTEIN MICHAEL HENRY/AU  
 E9 14 RUBINSTEIN MICHEL/AU  
 E10 2 RUBINSTEIN MIGUEL/AU  
 E11 3 RUBINSTEIN MORAN/AU  
 E12 1 RUBINSTEIN MORTON/AU

=> s e1

L8 251 "RUBINSTEIN MENACHEM"/AU

=> e cohen batya /au

E1 5 COHEN BAT SHEVA/AU  
 E2 3 COHEN BATIA/AU  
 E3 38 --> COHEN BATYA/AU  
 E4 1 COHEN BAZAIRE GERMAINE/AU  
 E5 79 COHEN BAZIRE G/AU  
 E6 42 COHEN BAZIRE GERMAINE/AU  
 E7 1 COHEN BEARAK A R/AU  
 E8 1 COHEN BEARAK ADENA/AU  
 E9 1 COHEN BEATRICE/AU  
 E10 1 COHEN BECKER E/AU  
 E11 3 COHEN BECKER I/AU  
 E12 13 COHEN BECKER I R/AU

=> s e3

L9 38 "COHEN BATYA"/AU

=> s l8 or l9

L10 269 L8 OR L9

=> s l10 and leptin

L11 16 L10 AND LEPTIN

=> s l11 and angiopoietin

L12 4 L11 AND ANGIOPOIETIN

=> dup rem l12

PROCESSING COMPLETED FOR L12

L13 3 DUP REM L12 (1 DUPLICATE REMOVED)

=> d l13 1-3 ti au py so

L13 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
 TI Method for determining leptin or leptin mimetic by  
 measurement of Ang-2, cellular RNA encoding Ang-2 or activation of Ang-2  
 promoter  
 IN Rubinstein, Menachem; Cohen, Batya  
 PY 2001  
 2001  
 2002  
 2002  
 2006



2003  
2003  
2004  
2006  
2006  
2006  
2003  
2002  
2004

SO PCT Int. Appl., 20 pp.  
CODEN: PIXXD2

L13 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN  
TI Leptin for use in inhibition of endothelial cell proliferation  
optionally together with VEGF inhibitors  
IN Rubinstein, Menachem; Cohen, Batya; Barkan, Dalit  
PY 2001  
2001  
2001  
2001  
2005  
2002  
2002  
2003  
2003  
2003  
2002  
2005

SO PCT Int. Appl., 38 pp.  
CODEN: PIXXD2

L13 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
TI Leptin induces angiopoietin-2 expression in adipose  
tissues  
AU Cohen, Batya; Barkan, Dalit; Levy, Yinon; Goldberg, Iris;  
Fridman, Eduard; Kopolovic, Juri; Rubinstein, Menachem  
PY 2001  
SO Journal of Biological Chemistry (2001), 276(11), 7697-7700  
CODEN: JBCHA3; ISSN: 0021-9258